THE INCIDENCE AND ANTI-MICROBIAL SENSITIVITY OF URINARY TRACT INFECTIONS IN HIV POSITIVE AND NEGATIVE NEPHROLOGY PATIENTS AT INKOSI ALBERT LUTHULI CENTRAL HOSPITAL IN KWAZULU NATAL PROVINCE, SOUTH AFRICA.

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Submitted in partial fulfilment of the requirements for the degree of Master of Medicine in Internal Medicine in the School of Nelson Rholihlahla Mandela School of Medicine, University of KwaZulu Natal.

August 2018

DECLARATION OF AUTHORSHIP

I, Dr Etheldreda Ivon Yoliswa Madela, declare that

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DEDICATION

For my daughter, Neo.

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CHAPTER 1

INTRODUCTION

INTRODUCTION

Nephrology unit at Inkosi Albert Luthuli Central hospital (IALCH) caters for all nephrology patients in the public sector in KwaZulu Natal province. This means there is always a list of patients waiting for bed availability in order to be transferred across to the unit. Most of these patients have been inpatients at other hospitals before transfer to the unit and some have had urinary catheters inserted at the referring hospitals, which increases their risk of urinary tract infections. All patients that are seen in the unit have urine dipsticks and urine microscopy culture and sensitivity done as part of the nephrology work up. Urinary tract infections (UTI) have become a challenge because most invasive procedures like renal biopsies are deferred in these patients until the infections have been cleared, which increases hospital stay for patients in the unit and longer waiting period for patients waiting beds. UTI can also worsen the renal function leading to early requirement for renal replacement therapy thereby increasing mortality and morbidity.

Early diagnosis and treatment of UTI is key on preventing complications but increasing resistance of the micro-organism causing UTI to the commonly used antibiotics, emergence of extended beta lactam (ESBL) resistance and multiple drug resistance (MDR) strains is a major challenge. It is therefore vital for health care facilities to be aware of the resistant strain and microbial sensitivity in their facility and communities in order to choose appropriate effective antibiotics.

LITERATURE REVIEW

UTI is among the most common causes of sepsis presenting in hospital. Forty to 50% of adult women have a history of at least one UTI. UTI is defined as the infection of the urinary system (see diagram below) which includes urethra, bladder (cystitis), ureter and kidneys (pyelonephritis) with a pathogen causing inflammation [1].

FIGURE 1 OF CHAPTER

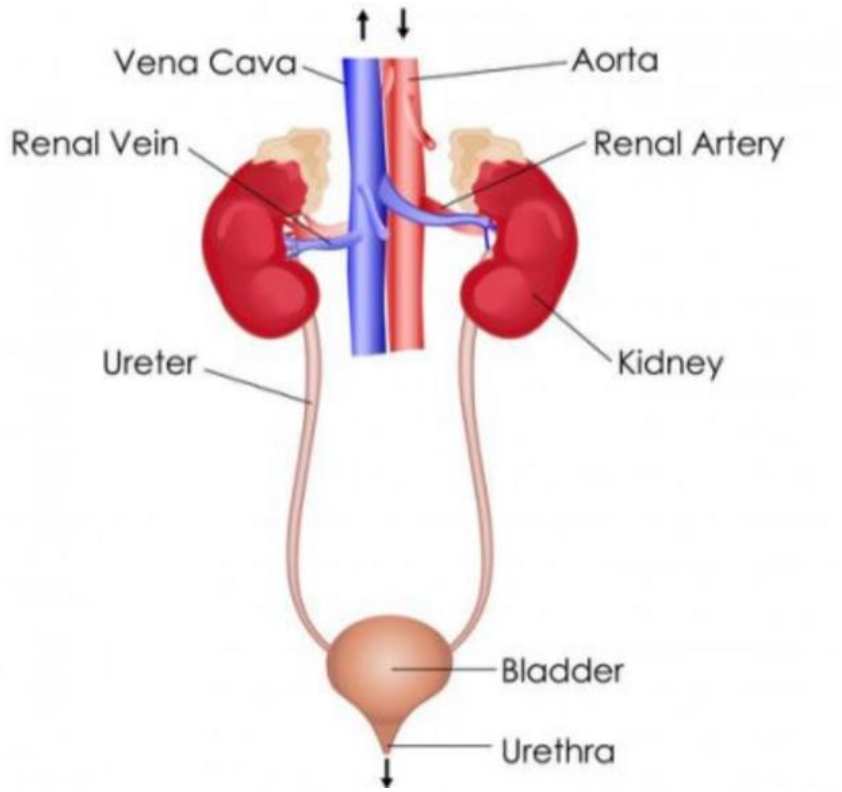

Diagram of the urinary system

Diagram from anatomyorgan.com

UTI can be symptomatic or asymptomatic (asymptomatic bacteriuria).Most micro-organisms colonize the colon, perianal region and periurethral and introitus region in females [2]. The frequency and severity of UTI is determined by local uroepithelial defense system and pathogenic factors of the micro-organisms. The common route of spread is ascension and the rate depends on effectiveness of the commensal flora in preventing colonization, local trauma such as in sexual activity and urethral massage, abnormalities of the urinary tract, diagnostic procedures, high vaginal pH and micro-

organism virulence factors.The virulence factors which ensure micro-organism survival include fimbriae, motility, glycocalyx-mediated adherence, urease production, production of haemolysin, somatic antigen expression and synthesis of aerobactin and enterobactin [1].

The risk of UTI is higher in elderly, pregnant women, immunocompromised, diabetic, post renal transplant, spinal injuries, patients admitted in the past three months, patients with urinary catheters and patients with urologic abnormalities [3-30]. Nephrology patients have most of these risk factors.

KwaZulu Natal province has the highest burden of HIV disease in the country[1].HIV infected patients have higher risk of acquiring kidney disease (acute or chronic) due to the effects HIV virus on the renal system, immune mediated mechanisms, risk of infections and side effects of antiretroviral therapy (ART).

HIV infected patients have been shown to have increased risk of UTI [3-6] , however this risk seem to be inversely proportional to the lymphocytes count or immune function of the patient [7-8]. There has not been a difference in the prevalence of bacterial growth between ART users and non-users, Escherichia coli (E. coli) is a predominant isolate [3-7, 9-11].

HIV positive patients on co-trimoxazole as a prophylaxis against pneumocystis carinni do not have reduced incidence of UTI as most studies have shown that most uropathogen are resistant to co-trimoxazole[12].

The increased risk of urinary tract infections in pregnancy is due to hormonal and mechanical changes on the urinary tract during pregnancy. Pregnant women with HIV and urinary tract infection had a higher rate of pre-labour rupture of membranes than HIV negative women with urinary tract infections[13-16]resulting in poor maternal and foetal outcomes.

Diabetes mellitus is a major cause of renal disease and patients with diabetes have high incidence of UTI [17-22]. This incidence is even higher in female patients with diabetes mellitus [23, 24]. This risk is explained by reduced T- cell mediated immune response, impaired bladder emptying [19] and defects in urinary cytokines secretion [25] in patients with diabetes mellitus. These patients do not only have high risk of acquiring UTI but

also increased complications associated with it [19-21, 24].

Patients with SLE are often seen in nephrology with Lupus nephritis. Patients with SLE have higher incidence of bacterial and mycotic infection compared to patients with Rheumatoid arthritis and Nephrotic syndrome [26-28] with even higher incidence of UTI [29]. This is due to low antibody response, defective phagocytosis, decreased leucocytes chemotaxis, decreased lymphocyte toxic serum factors, selective defect on cellular immunity and delayed hypersensitivity response [26].

UTI is the most common complication after renal transplant [30] with ABU being the most common manifestation [31]. UTI is associated with impairment in allograft function [30].

E. coli is the most common cause of UTI in community acquired, hospital acquired, pregnant, HIV positive and negative, Diabetic, SLE and post renal transplant cohorts of patients [3-21, 29, 30, 32].

E. coli is the predominant isolate in UTI in South Africa [33], continent of Africa [34-39] and the rest of the world [16, 40-41]. Enterobacteriaceae, Klebsiella, but Pseudomonas aeruginosa, Enterococci, Staphylococci, and fungi are also significant causes [42].

Treating urinary tract infections has become a challenge due to increasing resistance to antibiotics [32, 42-45]. There is consensus among different studies about increasing resistance of UTI to the commonly used antibiotics. There is also increasing rates of multi drug resistance [46, 47] and ESBL positive organisms [48, 49, 50]. The recent data from Lancet laboratories in KZN region for a period 1 August 2017 to 13 July 2018 shows 20% ESBL positive E.coli and 40% ESBL positive K. pneumonia.

The increasing resistance has been mainly noted against Ciprofloxacin, Co-trimoxazole and Amoxicillin/clavulanate [34, 36,50-53]. Nitrofurantoin sensitivity remains high with low resistance of 0% resistance in a study done in Germany [50].

In a Study at 3 Military Hospital in Bloemfontein, South Africa, E. coli was the most cultured organism but it was resistant to mostly used antibiotics hence stressing the need to constantly revise empiric use of antibiotics[32]

In an anti-microbial susceptibility study on Escherichia coli done in South African

public and private sector from 2007 to 2011 there was statistically significant changes in antimicrobial susceptibility noted for many antibiotics. There was a small increase in Ampicillin susceptibility but resistance to it was too high to allow its use as empiric therapy and there was a significant decline in Amikacin susceptibility but overall susceptibility remained above 95%. This means that for now, Amikacin can be used to treat pyelonephritis. Amikacin toxicity and the requirement for parenteral administration are drawbacks to its use. There was consistent and progressive decline in susceptibility to Cephalosporins and Fluoroquinolones, on both a national and local level. Susceptibility to Fluoroquinolones was between 70-86% at different laboratories in 2011, making it a major concern as these are first-line drugs that are recommended internationally and in the locally used Essential Drug List, and are widely used in public and private sectors [54].

The antibiotics with the highest activities in 2011 were: broad-spectrum cephalosporins, Imipenem, Ciprofloxacin, Amikacin, and Fosfomycin, followed by Cefoxitin, Cephalothin, Amoxicillin-clavulanic acid, Gentamicin, Tobramycin, Nalidixic acid, Co-trimoxazole, and Nitrofurantoin. Fosfomycin exhibited high activity against most Enterobacteriaceae isolates [45, 54]

Susceptibility to nitrofurantoin was above 90% and the advantage to its use was the limited impact on the normal gut flora [52, 54]. Five years later there has been a significant decline in activity of the antibiotics which had high sensitivity in 2011 as evident in the recent Lancet Laboratory statistics in KZN region from 2017 to 2018 (see Table 1).

TABLE 1

Table provided by Dr Abdool Peer from Lancet laboratories.

STATISTICS FROM KZN REGION ONLY: 1 AUGUST 2017 TO 13 JULY 2018: UNPUBLISHED DATA.

	E. coli (% susceptible)	**K. pneumonia (% susceptible)**
Amikacin	99	95
Ampicillin	23	4
Augmentin	77	58
Co-trimoxazole	43	49

Fosfomycin	96	90
Ciprofloxacin	64	64
Nitrofurantoin	98	83

Prevention of UTI remains vital in reducing mortality and morbidity especially in the vulnerable groups. This includes improving patient's immune status and controlling underlying medical condition, reducing routine catheterisation unless absolutely indicated, reducing duration of catheterization and intermittent catheterization which has been shown to reduce UTIs [55, 56]. Antibiotic cycling has been used to prevent recurring UTIs in patients with neurogenic bladder [56]. Vaginal oestrogens restore the vaginal lactobacilli flora, reducing colonization with Enterocteriaceae in postmenopausal women [57]. Cranberry products have also been shown to reduce the recurrence of UTIs by 30-40% in perimenopausal women but optimal dose is yet to be determined [57, 58].

RATIONALE FOR CONDUCTING THIS STUDY

1. The risk of acquiring UTI is high in nephrology and HIV infected patients. This risk should be even higher in HIV infected nephrology patients but there is limited literature on the incidence and antimicrobial sensitivity in nephrology patients specifically. This study was done to fill that gap in the literature.
2. With the rising incidence of ESBL and MDR strains on UTI, it was important for us to be aware of the extent of microbial resistance and the antibiotics we use in our institution.

RESEARCH QUESTION

What is the incidence and antimicrobial susceptibility of urinary tract infection in HIV negative and positive nephrology patients?

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CHAPTER 2

2.1 THE INCIDENCE AND ANTI-MICROBIAL SENSITIVITY OF URINARY TRACT INFECTIONS IN HIV POSITIVE AND NEGATIVE NEPHROLOGY PATIENTS AT INKOSI ALBERT LUTHULI CENTRAL HOSPITAL IN KWAZULU NATAL PROVINCE, SOUTH AFRICA.

Prepared according to the Instructions for Authors of South African Medical Journal

2.2 LIST OF ABBREVIATIONS

ART	Antiretroviral therapy
BREC	Biomedical Research Ethics Committee
ESBL	Extended spectrum beta lactam
E. coli	Escherichia coli
HIV	Human immunodeficiency virus
IALCH	Inkosi Albert Luthuli Central Hospital
UTI	Urinary tract infection
K. pneumonia	Klebsiella pneumonia
KZN	KwaZulu Natal province
SLE	Systemic Lupus Erythematosus

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2.4 ABSTRACT

Background: Urinary tract infection is among the most common causes of sepsis presenting in hospitals. The aim was to collect data to enable empirical treatment of urinary tract infections in HIV negative and positive nephrology patients while waiting for urine culture results in order to reduce hospital stay.

Objectives: To assess incidence and antimicrobial susceptibility of urinary tract infections in HIV negative and positive patients.

Methods: A retrospective chart review of nephrology patients admitted from January to December 2014 in Nephrology ward and the first consecutive 200 outpatients seen in Nephrology clinic in 2014 at Inkosi Albert Luthuli Central Hospital was conducted. Information was gathered with the use of a data collection sheet and urinary tract infection was based on urine culture results. . All data was analysed using Statistical Package for Social Sciences version 23. Percentages of basic characteristics were calculated between groups, Logistic regression analysis was used to identify factors associated with positive urine culture.

Results: There were 654 patients in the study, 514 (79%) were HIV negative and 139 (21%) were HIV positive. The incidence of UTI in nephrology patients was 9%, 10.1% in inpatients and 6.5% in outpatients. 22% were HIV positive (p value 0.883, 95% CI 0.550-2.003). 19% had Diabetes mellitus, 15% had Systemic Lupus Erythematosus and 5% were post renal transplant patients. Escherichia coli and Klebsiella pneumonia were the common causes of urinary tract infection at 40.7% and 15.3% respectively with 22% cases on extended beta lactam resistance.

Conclusions: There was no statistically significant difference on the incidence and anti-microbial isolates between HIV infected and HIV negative nephrology patients with urinary tract infection. Escherichia coli and Klebsiella pneumoniae were the most commonly cultured organisms in both groups. There is microbial resistance to commonly used antibiotics.

Recommendations: Constant assessment of anti-microbial sensitivity of urinary tract infections is of paramount importance.

2.5 INTRODUCTION

Urinary tract infection (UTI) is an infection of the urinary system which includes urethra, bladder (cystitis), ureter and kidneys (pyelonephritis). It can be symptomatic or asymptomatic bacteriuria (ABU).
The risk of urinary tract infection is higher in elderly, pregnant women, immunocompromised, diabetic, post renal transplant, post spinal injuries, patients admitted in the past three months, patients with urinary catheters and patients with urologic abnormalities. Nephrology patients have most of these risk factors.

Nephrology unit at Inkosi Albert Luthuli Central hospital (IALCH) caters for all nephrology patients in the public sector in KwaZulu Natal province (KZN). This means there is always a list of patients waiting for bed availability in order to be transferred across to the unit. Most of these patients have been inpatients at other hospitals before transfer to the unit and some have had urinary catheters inserted at the referring hospitals, which increases their risk of urinary tract infections. All patients that are seen in the unit have urine dipsticks and urine microscopy culture and sensitivity done as part of the nephrology work up. UTI can worsen the renal function leading to early requirement for renal replacement therapy (RRT) thereby increasing mortality and morbidity, delays invasive procedures and increases hospital stay. This leads to longer waiting period for beds. It is therefore of paramount importance that the unit is aware of the incidence and antimicrobial susceptibility of the UTIs for early treatment and prevention of complications associated with UTIs.

KZN has the highest burden of HIV disease in the South Africa [1]. HIV infected patients have higher risk of acquiring kidney disease (acute or chronic) due to the effects HIV virus on the renal system, immune mediated mechanisms, risk of infections and side effects of antiretroviral therapy (ART). HIV infected patients have been shown to have increased risk of UTI [2-4].
Patients with diabetes mellitus, systemic lupus erythematosus (SLE) and post renal transplant have higher risk of acquiring both kidney disease and UTI and are mostly susceptible to complications associated with it [7-20].

Escherichia coli (E. coli) is the most common cause of UTI in community acquired, hospital acquired, pregnant, HIV positive and negative, Diabetic, SLE and post renal transplant cohorts of patients[2-7, 20-21].

E. coli is the predominant isolate in UTI in South Africa [21, 22], continent of Africa [23-28] and the rest of the world [29-31].

Enterobacteriaceae, Klebsiella, Pseudomonas aeruginosa, Enterococci, Staphylococci, and fungi are also significant causes [32].

Early diagnosis and treatment of UTI is key on preventing complications but increasing resistance of the micro-organism causing UTI to the commonly used antibiotics, emergence of extended beta lactam resistance (ESBL) and multiple drug resistance (MDR) strains is a major challenge [32-36]. It is therefore vital for health care facilities to be aware of the resistant strain and microbial sensitivity in their facility in order to choose appropriate effective antibiotics.

Prevention strategies include restricting insertion of urinary catheters unless absolutely indicated, intermittent catheterization, vaginal oestrogens for perimenopausal women and use of cranberry products in high risk patients [36-38].

There is limited data on the incidence and antimicrobial susceptibility in HIV negative and positive nephrology patients specifically, the objective of the study was to bridge that gap and to be able to choose appropriate treatment early in our facility in order to prevent morbidity and mortality.

2.6 METHODS

This is a retrospective chart review of nephrology patients seen in 2014. The study protocol was approved by Biomedical Research Ethics Committee (BREC) reference number BE496/15, Department of Health reference number HRKM049/17 and IALCH CEO.

The study included all nephrology patients admitted at IALCH from January to December 2014 and the first 200 out of 5843 outpatients (CI 95%, margin of error 6.9%, proportion estimate 50%) seen in nephrology clinic in 2014. Only the first admission was considered for patients who were admitted more than once in the same year. Patient's medical chart and laboratory records were reviewed to obtain demographics, HIV status, underlying renal disease and urine culture.

Patients were divided into two groups based on HIV status as documented on the chart or laboratory results. CD4 count and viral load was obtained from laboratory results for all the HIV positive patients

UTI was based on positive urine culture results. Patients with positive urine culture had their charts reviewed further for symptoms, signs, dipstick, urine sensitivity and treatment given. All data was gathered using a data collection sheet.

The data collected was captured and analysed using the Statistical Package for Social Sciences (SPSS version 23). Percentages of basic characteristics were calculated and comparative percentages between groups (i. e HIV negative and HIV positive) were performed. Logistic regression analysis was used to identify factors associated with positive urine culture. All tests of significance were two-sided and a confidence interval of 95% was accepted.

2.7 RESULTS

Baseline characteristics of patients

TABLE **2** demonstrates the baseline characteristics and urine culture of HIV positive and negative patients included in the study; there were 59 (9%) patients with confirmed UTI, 46 (78%) inpatients and 13 (22%) outpatients, 43 (73%) females and 16 (27%) males. 46 (78%) were HIV negative and 13 (22%) of patients were HIV positive.
E. coli was cultured in 24 (40.7%) patients, 6 (46.1%) HIV positive and 18 (39.1%) HIV negative while K. Pneumonia was cultured in 9 (15.3%) of the patients, 2 (15.4%) HIV positive and 7 (15.2%) HIV negative.
47 (79.7%) of the patients had no urinary symptoms recorded, 8 (13.6%) presented with fever, 2 (3.4%) had dysuria and 2 (3.4%) had flank pain. 44 (74.6%) had no signs, 8 (13.6%) had tachycardia, 6 (10.2%) had pyrexia, and 1 (1.7%) had suprapubic tenderness.

The incidence of UTI was 10.1% and 6.5% among inpatients and outpatients respectively (see Table 3).
Table 3 shows sample size and distribution of patients; there were 654 patients in total, 815 were admissions of which 361 were re-admissions, one admission per patient was counted giving total of 454 inpatients and 200 outpatients
The mean age was 42 (11-78).
Out of the 654 patients, 515 (79%) were HIV negative and 139 (21%) HIV positive of which 127 (91%) were on ART, 11 (8%) not on ART, 1 (1%) unknown.

UTI risk factors

In a multivariate analysis the risk factors associated with UTI in nephrology patients were HIV infection (95% CI, 0.883 0.550-2.003; p 0.883), diabetes mellitus (95% CI, 0.187-0.107; p 0.332), SLE (95% CI, 0.020-0.38; p 0.35) and post renal transplant (95% CI, 0.040-0.089; p 0.208) see Table 4.
11 (85%) of the HIV positive patients were on ART, 2 (15%) were not on ART, the mean CD4 count was 318 (65-561) and viral load 1607845 (199-10000000).

Urinalysis

Table 5 shows urinalysis findings on the patients with positive urine culture, protein was the predominant finding in 80% of the patients, blood was in 70.9%, leucocytes in 32.7% and nitrites in 10.9%.

TABLE 2: BASELINE CHARACTERISTICS OF PATIENTS INCLUDED IN THE STUDY

	HIV positive	**HIV negative**	**p value**
No of patients n = 59	n=13 (22%)	n=46 (78%)	0.883
Gender			
Females = 43 (73%)	9 (69.2%)	34 (73.9%)	1.000
Males = 16 (27%)	4 (30.8%)	12 (26.1%)	0.749
In/outpatients			
Inpatients = 46 (78%)	11 (84.6%)	35 (76.1%)	0.817
Outpatients = 13 (22%)	2 (15.4%)	11 (23.9%)	0.723
Diabetes mellitus = 11 (19%)	1 (7.6%)	10 (21.7%)	0.442
SLE = 9 (15%)	0	9 (19.5%)	0.189
Post renal transplant = 3 (5%)	0	3 (6.5%)	1.000
Symptoms			
Asymptomatic = 47 (79.7%)	10 (76.9%)	37 (80.4%)	1.000
Fever = 8 (13.6%)	1 (7.7%)	7 (15.2%)	1.000
Dysuria = 2 (3.4 %)	0	2 (4.3%)	1.000
Flank pain = 2 (3.4 %)	2 (15.4%)	0	1.000
Signs			
No signs = 44 (74.6%)	9 (69.2)	35 (76.1%)	1.000
Tachycardia = 10 (16.9%)	3 (23.1)	7 (15.2%)	0.687
Pyrexia = 6 (10.2%)	1 (7.7%0	5 (10.9%)	1.000
Suprapubic tenderness = 1 (1.7%)	1 (7.7%)	0	0.233
Microbial isolates			
Escherichia coli = 24 (40.7%)	6 (46, 1%)	18 (39.1%)	0.779
Klebsiella pneumonia = 9 (15.3%)	2 (15.4%)	7 (15.2%)	1.000
Enterococcus fecalis = 5 (8.5%)	1 (7.7%)	4 (8.7%)	1.000
Candida albicans = 4 (6.8%)	1 (7.7%)	3 (6.5%)	1.000
Acinobacter baumanni = 4 (6.8%)	0	4 (8.7%)	0.572

Pseudomonas aeruginosa = 3 (5.1%)	1 (7.7%)	2 (4.3%)	0.543
Streptococcus agalactiea = 2 (3.4%)	0	2 (4.3%)	1.000
Enterobacter feacalis = 1 (1.7%)	1 (7.7%)	0	0.233
Enterococcus cloacae = 1 (1.7%)	1 (7.7%)	0	0.233
Staphylococcus aureus = 1 (1.7%)	0	1 (2.2%)	1.000
Proteus vulgaris = 1 (1.7%)	0	1 (2.2%)	1.000
Proteus mirabis = 1 (1.7%)	0	1 (2.2%0	1.000
Serratia marcescens = 1 (1.7%)	0	1 (2.2%)	1.000

TABLE 3: SAMPLE SIZE AND DISTRIBUTION OF PATIENTS

	Inpatients	**Outpatients**	**p value**
N=654	454	200	
UTI= 59 (9%)	46	13	0.184
Incidence %	10.1%	6.5%	

TABLE 4: UTI RISK FACTORS IN NEPHROLOGY PATIENTS

	HIV infected	**Diabetes mellitus**	**Systemic Lupus Erythematosus**	**Post renal transplant**
All patients N=654	139 21%	115 24%	56 9%	17 3%
UTI patients n=59	13 22%	11 19%	9 15%	3 5%
p value* 95% CI	0.883	0.332	0.034	0.208

*p values obtained using Pearson Chi- Square test

TABLE 5: DIPSTICK OF PATIENTS WITH UTI

	Protein	**Blood**	**Leucocytes**	**Nitrites**
n= 59	44	39	18	6
%/100	80%	70.9%	32.7%	10.9%

Microbial sensitivity

Escherichia coli and Klebsiella pneumonia

Table 6 shows sensitivity and resistance patterns of the commonly cultured organisms, E. coli 24 (40.7%) and K.pneumonia 9 (15.3%).

E coli was mostly sensitive to Nitrofurantoin in 18 (75%) and Amoxicillin/ clavulanate in 13 (54.2%) and resistant to Co-trimoxazole in 11 (45.8%) and Ciprofloxacin in 9 (35.7%).

K. pneumonia was mostly sensitive to Meropenem/ imipenem in 5 (55.6%) and Amikacin in 4 (44.4%). It was resistant to Ciprofloxacillin in 7 (77.8%) and Co-trimoxazole in 5 (55.6%). K. pneumonia also had 2 (22.2%) of cases with ESBL resistant organisms.

Sensitivity and resistance was not reported against all the antibiotics in Table 6, i.e. E. coli was sensitive to Ciprofloxacin in 7 patients and resistant in 9 patients. There was no Ciprofloxacin sensitivity done for the other 8 patient who cultured E. coli.

Candida albicans

Candida albicans was cultured in 4 (6.8%) of patients and 3 (75%) were sensitive to Fluconazole with 1 (25%) case of resistance.

TABLE 6: E. COLI AND K. PNEUMONIA SENSITIVITY AND RESISTANCE

Antibiotic	**E. coli sensitivity**	**E. coli resistance**	**E. coli sensitivity/ resistance not reported**	**K. pneumonia sensitivity**	**K. pneumonia resistance**	**K. pneumonia sensitivity/ resistance not reported**
Ciprofloxacin	7 (29.2%)	9 (37.5%)	8 (33.3%)	2 (22.2%)	7 (77.8%)	-
Amoxicillin / clavulanate	13 (54.2%)	3 (12.5%)	8 (33.3%)	3 (33.3%)	3 (33.3%)	2 (22.2%)
Nitrofurantoin	18 (75%)	-	6 (25%)	-	-	9 (100%)
Meropenem/ Imipenem	5 (20.8%)	-	21 (87.5%)	5 (55.6%)	-	4 (44.4%)
Trimethoprim/ sulfamethoxaz	-	11 (45.8%)	13 (54.2%)	-	5 (55.6%)	4 (44.4%)

ole						
Amikacin	-	-	24 (100%)	4 (44.4%)	-	5 (55.6%)
ESBL	-	0		-	2 (22.2%)	

Antibiotics used

Table 7 shows a record of antibiotics used on the 59 patients with positive urine culture, 27 (45.8%) unknown includes patients who were managed as ABU and patients that were transferred back to referring hospitals before initiation of any antibiotic.

TABLE 7: ANTIBIOTICS USED

Antibiotic	**N=59 / %= 100**	
Unknown*	27	45.8%
Ciprofloxacillin	10	16.9%
Amoxicillin/clavulanate	9	15.3%
Meropenem or Imipenem	9	15.3%
Vancomycin	2	3.4%
Cloxacillin	1	1.7%
Colistin	1	1.7%

*ABU and patients with no record of antibiotics in the case notes.

2.8 DISCUSSION

There was no statistical difference on incidence of UTI and microbial isolates between HIV negative and positive nephrology patients. This is probably due to the fact that HIV positive nephrology patients are required to be on ART for at least six months or have a suppressed viral load to be accepted to the renal program as per the South African National guidelines. The risk of UTI in HIV infected patients is related to immune function determined by lymphocyte count [39-40] and ART improve immune function. The HIV positive were compared to the HIV negative but 50% of the HIV negative in this study also had some form of immune suppression i.e. patients with diabetes mellitus, SLE and post renal transplant (see TABLE 2) which could explain the lack of significant difference between the two groups.

The incidence of UTI in patient with diabetes mellitus of 19% (Table 4) was similar to the 19.5% reported in Sudan [5] and lower than the 25.3% in Saudi Arabia [9]. The incidence of UTI among post renal transplant was 5% (Table 4) which is lower than the 25% and 26-76% reported in previous studies [20]. This could be attributed to the small (3%) number of post renal transplant patients in this study.

E. coli and K. pneumonia were the most commonly cultured organisms in both HIV negative and positive patients (see TABLE **2**), this is in contrast with a study done in Poland in which 1/3 of HIV infected patient cultured non-typical organisms [41]. This difference could be explained by the fact that 85% of the HIV positive patients in our study were on ART.

E. coli was the most cultured organism at 40, 7% (TABLE 2) across all groups. It is the most common cause of UTI across all groups in literature, in Africa [23-28] and the rest of the World [29-31].

E.coli and K. pneumonia resistance was mostly to Ciprofloxacin at 37.5% and 77.8%, Amoxicillin/clavulanate at 12.5% and 33.3% and Co-trimoxazole at 45.8% and 55.6% respectively. This was not different from the previous studies done in South Africa, Congo and Uganda [23, 25, 41-43]. This is a major concern as these are widely used first line drugs against UTIs.

The antibiotic of choice for empiric treatment in our unit would be Amoxicillin/

clavulanate as it has better sensitivity and less resistance when compared to Ciprofloxacin.
The 22% of ESBL resistant K. pneumonia cultured in nephrology patients in 2014 has increased to 40% reported by Lancet laboratories in KZN in 2018 which is a major concern and stresses the need for constant assessment of anti-microbial culture and sensitivity of UTI.

In this study we have shown the role of ART in reducing the risk of UTI in HIV positive nephrology patients as evidenced by a lack of significant difference in the incidence of UTI between HIV negative and positive patients.
Previous studies were prior to the ART era, more studies are needed to assess the impact of ART and CD4 count on the development of UTI.
Previous studies done on UTI focused mainly on pregnant women, urology patients and patients with spinal conditions and preventative strategies have been focused mainly on those groups. This study has highlighted that nephrology patients are also susceptible to UTI, compared to the general population. Therefore research on the impact of preventative strategies used for the other high risk groups would be beneficial in nephrology patients as well.
The limitations in our study were that it was a retrospective study done in a specialised unit with limited number of patients and all data was dependent on information documented in the patient's clinical records.
Some cultured organisms did not have drug sensitivity done on all the drugs making exact resistance percentage difficult to assess. Some patients were transferred back to referring hospitals before initiation or completion of treatment therefore the outcomes could not be assessed.
Constant research on this field would be beneficial especially now with the emergence of MDR and ESBL resistant organisms.

2.9 CONCLUSION

Urinary tract infections are the commonest infections in out and inpatient settings. HIV positive, diabetes mellitus, SLE and post renal transplant cohorts of patients are nephrology patients which are mostly susceptible to UTIs. Delays in treating UTI may worsen the renal function leading to early renal replacement therapy and delays invasive procedures thus increasing morbidity and mortality.

E. coli is the commonest cause of UTI in both HIV negative and positive nephrology patients.

There is need for constant assessment of anti-microbial sensitivity of UTI due to increasing microbial resistance to commonly used antibiotics by the common organism and increasing number of MDR and ESBL resistant organisms.

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CHAPTER 3

APPENDICES

3.1 Data collection sheet

3.2 BREC approval and extension approval

3.3 IALCH consent

3.4 DoH approval